Population Data, Ethics and Paediatric Care:

How we can use population data to guide ethical decision making

PAEDIATRIC GRAND ROUNDS
Riley Hospital for Children

Professor Fiona Stanley AC

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Executive Director Australian Research Alliance for Children and Youth

Audrey Pratt Visiting Professor in Paediatric Bioethics

13 June 2007

Population of Western Australia:

2 Million

Population of Australia:

20.2 Million

TELETHON INSTITUTE FOR CHILD HEALTH RESEARCH

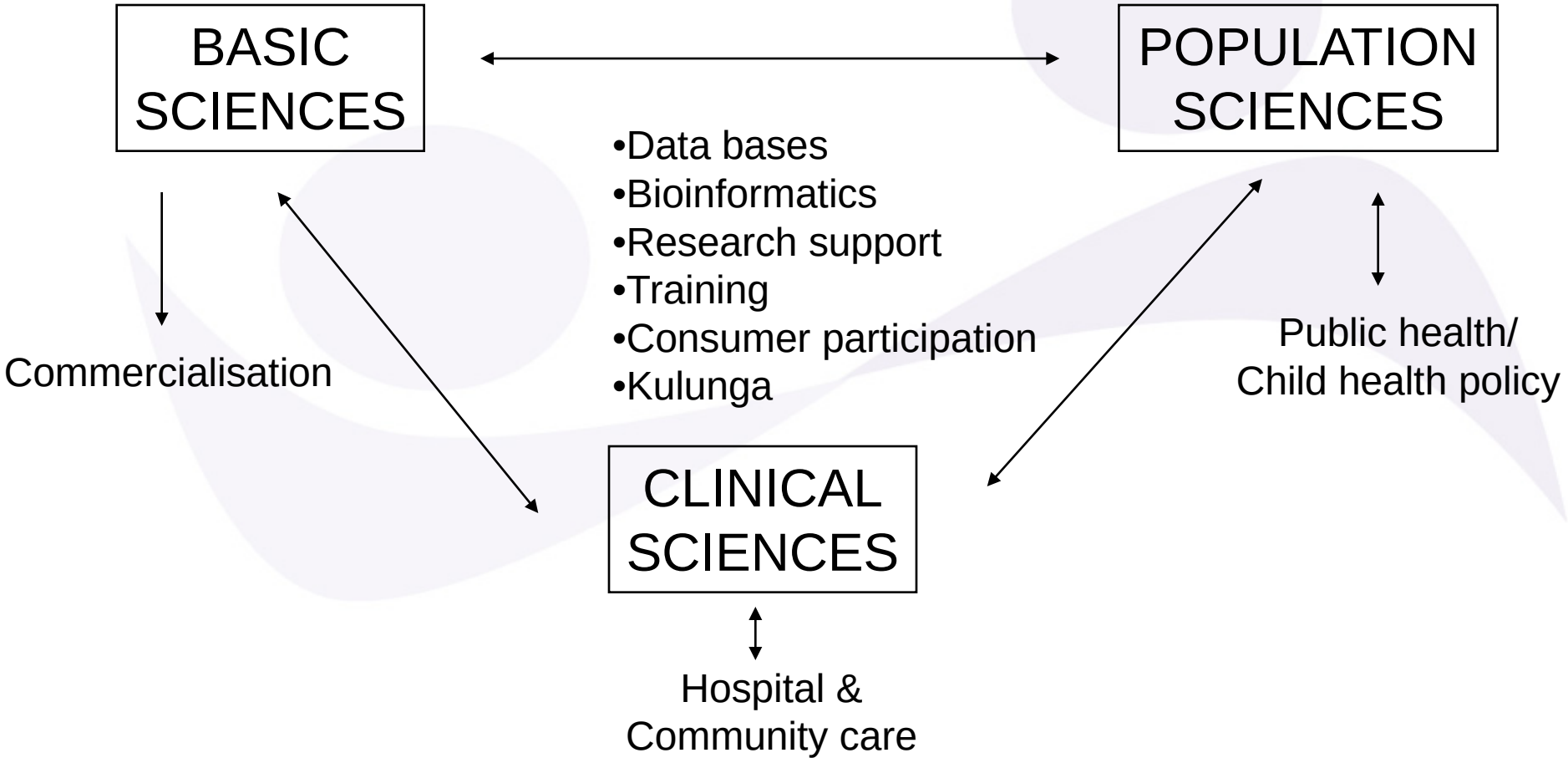
Our Mission

'To improve and promote the health and well being of all children through the unique application of multi disciplinary research'

Aims:

- To conduct high quality research
- To apply research findings to improve the health of children, adolescents and families
- To teach the next generation of health researchers.
- To be an advocate for research and for children

ICHR Philosophy



LOCAL, NATIONAL & INTERNATIONAL COLLABORATIONS

Research Themes

- Aboriginal child health
- Asthma, allergies & respiratory diseases
- Cancer & leukaemia
- Developmental disorders (BD, CP,ID)
- Infectious diseases
- Mental health
- Developmental origins of health & disease

Australian Research Alliance for Children and Youth

A national collaboration established to facilitate, coordinate and support the development of knowledge and its effective use to enhance the well-being and life chances of children and young people.

Outline

1. Population data and record linkage in WA
   A) Development/ methods/ advantages
   B) Examples for child health services
2. The special case of pharmacovigilance
3. Ethical issues
4. Modernity's paradox and the imperative for good data

1. Population Data & Record Linkage in WA

A) Development/ methods/ advantages
B) Examples for child health/ services

WA Maternal and Child Health Research Data Base 1977-2004

1970's

- Public concerns re thalidomide and adverse effects of perinatal care

1980/81

- Establish 1st Australian linkage of births, deaths and midwives (perinatal) records (total population)
- Establish registers of cerebral palsies and birth defects to link to data base

1982/83

- Link computerised hospitalisations

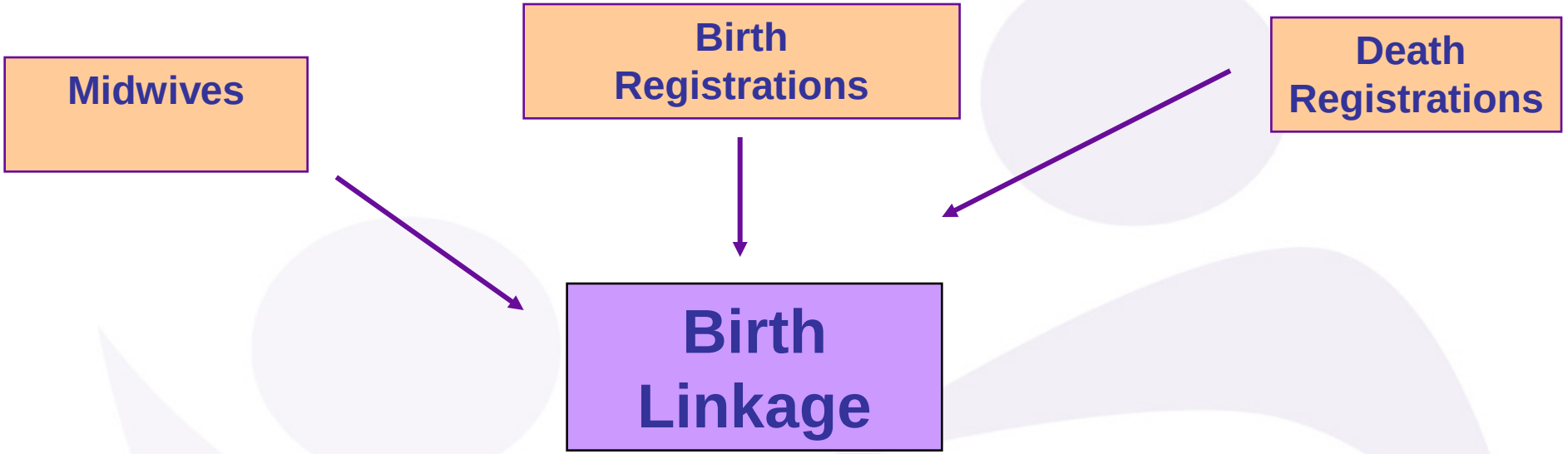
1990 onwards

- Ongoing MCHRDB

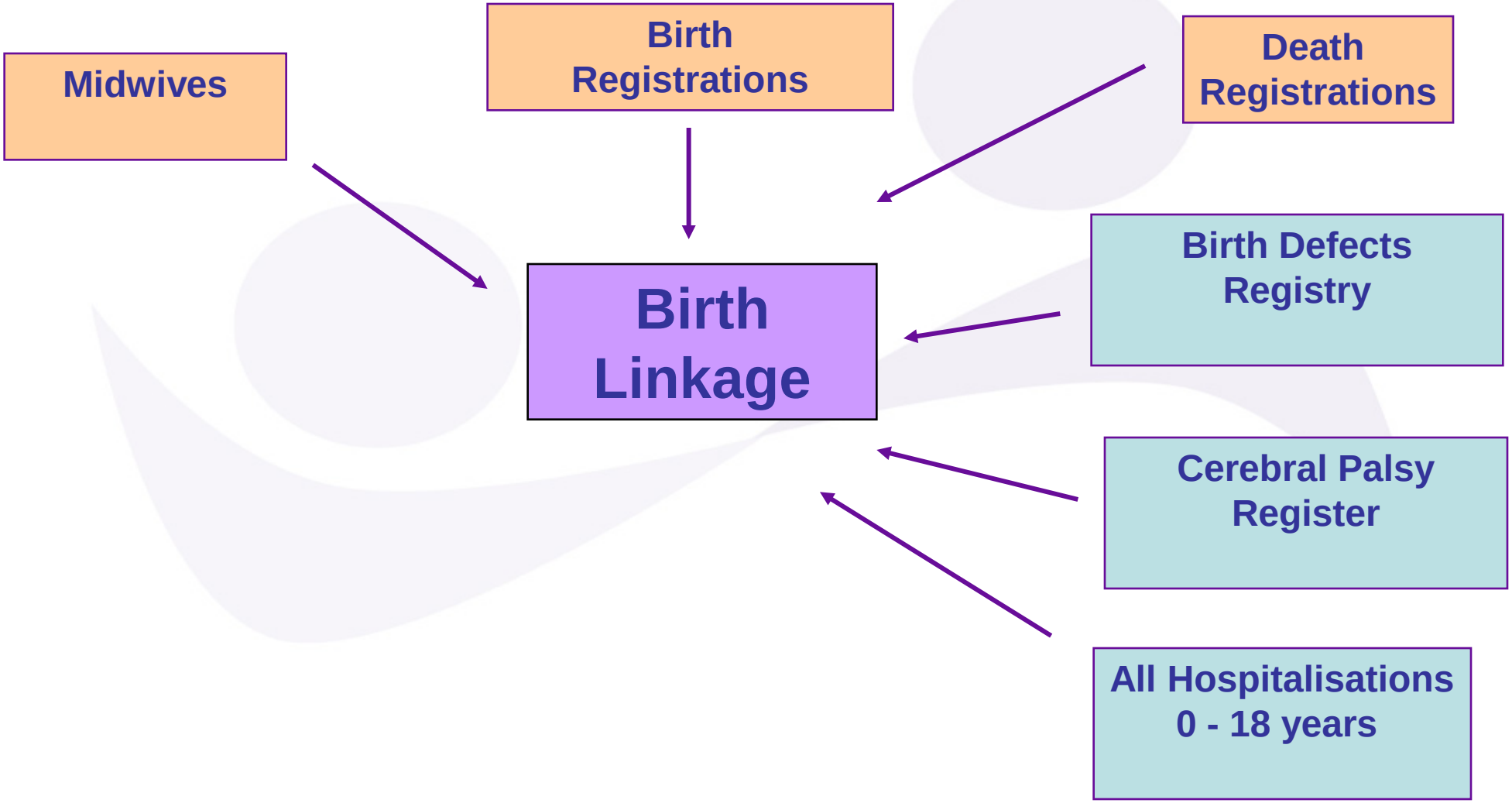
2004

- WA data linkage system

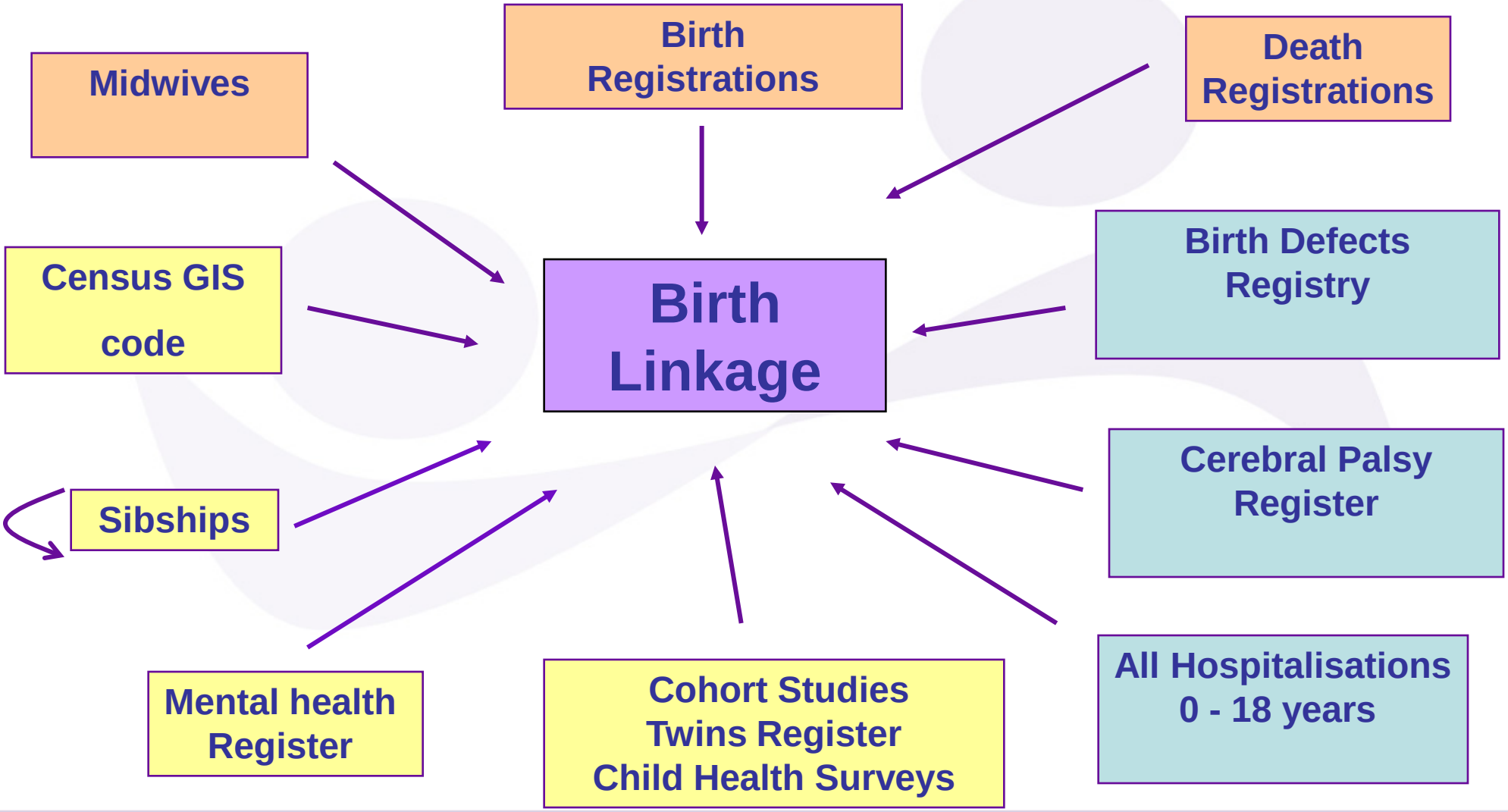
Maternal and Child Health Research Database 1980-2003



Maternal and Child Health Research Database 1980-2003



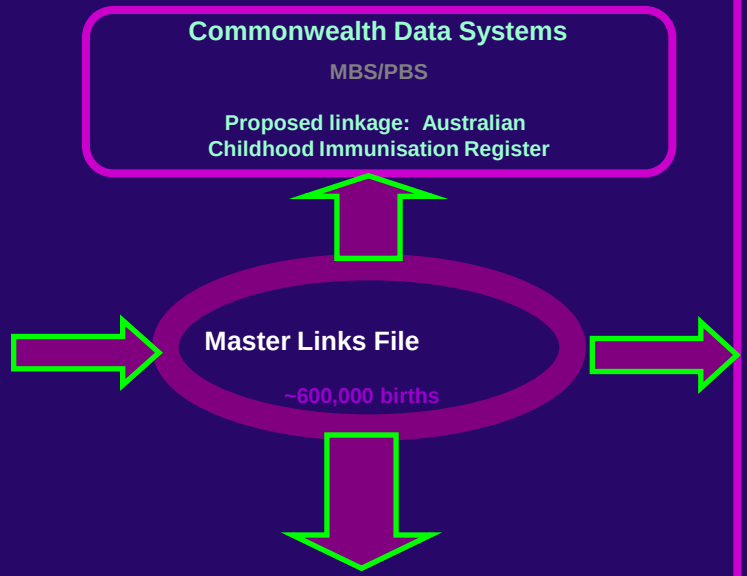
Maternal and Child Health Research Database 1980-2003



Population databases which can provide data for research

Core Data Sets

- Birth Registrations 1974+
- Death Registrations 1969+
- Hospital Separations 1970+
- Midwives' Notifications 1980+
- Birth Defects 1980+
- Geocoding, socio-economic indices 1986+



Research Databases

Institute for Child Health Research

- Snapshot of Maternal & Child Health Research Data Base
- WA Pregnancy Cohort 1989-92
- WA Child Health Survey WA Aboriginal Child Health Survey 2001-2
- WA Twin Register 1980+ →
- RASCALS 1995-6
- Sibships 1980+1993
- Invasive Pneumococcal Disease 1996+ →
- Intellectual Disability 1980+ →
- Cerebral palsy 1956+ →
- Autism 1999+ →
- Newborn Encephalopathy 1995-7

Other

Based on and consistent with the WA DATA LINKAGE SYSTEM, February 2004

Advantages of WA Population Data & Record Linkage

eg MCHRDB

- 100% sample: unbiased, no one excluded
- Cheap cf. seeking consent/ surveys
- Valid & reliable data on sensitive issues
- Reduces survey burden on populations
- Fast, effective linkage technology
- Privacy protected
- Better data for policy, planning, evaluation
- Improve administrative data

Limitations of WA Population Data & Record Linkage

- Information only available on items and outcomes recorded in data bases (breadth > depth)
- Privacy issues still need to be addressed eg ethics committees, understanding of public good by the community
- Need better, complete denominators
- Changes in diagnostic classifications present challenges for temporal analyses
- (In)accuracy of recorded information
- Incomplete ascertainment
- Sample size for rare disorders (APSU)

Antenatal Factors in Later Disease/ Disability

- Trends in diseases & disability (complete)
- Environmental exposures & later diseases
- Birth outcomes in psychiatric patients
- Intra-uterine growth & later development (DOHaD)
- Pregnancy problems & later childhood diseases
- Reproduction and subsequent maternal health

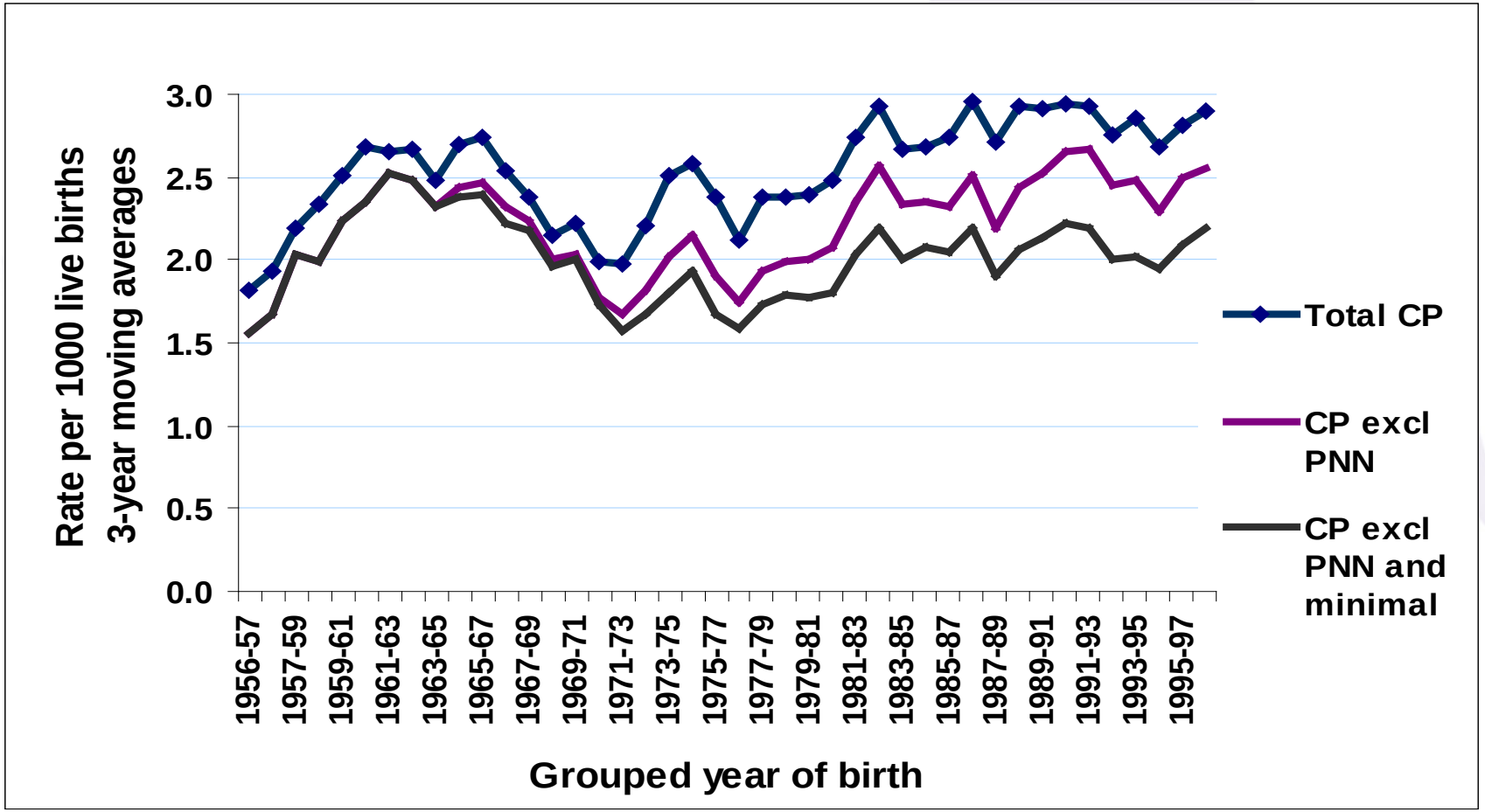
Evaluation of Medical Care

- Increased very preterm survival - problems in survivors
- IVF & cerebral palsy, disabilities
- IVF & birth defects
- Reasons for and impact of, increasing caesarean sections
- Effects of increased obstetric intervention
- Adverse drug effects (pharmacovigilance)
- Clinical audit

Evaluation of Health Promotion

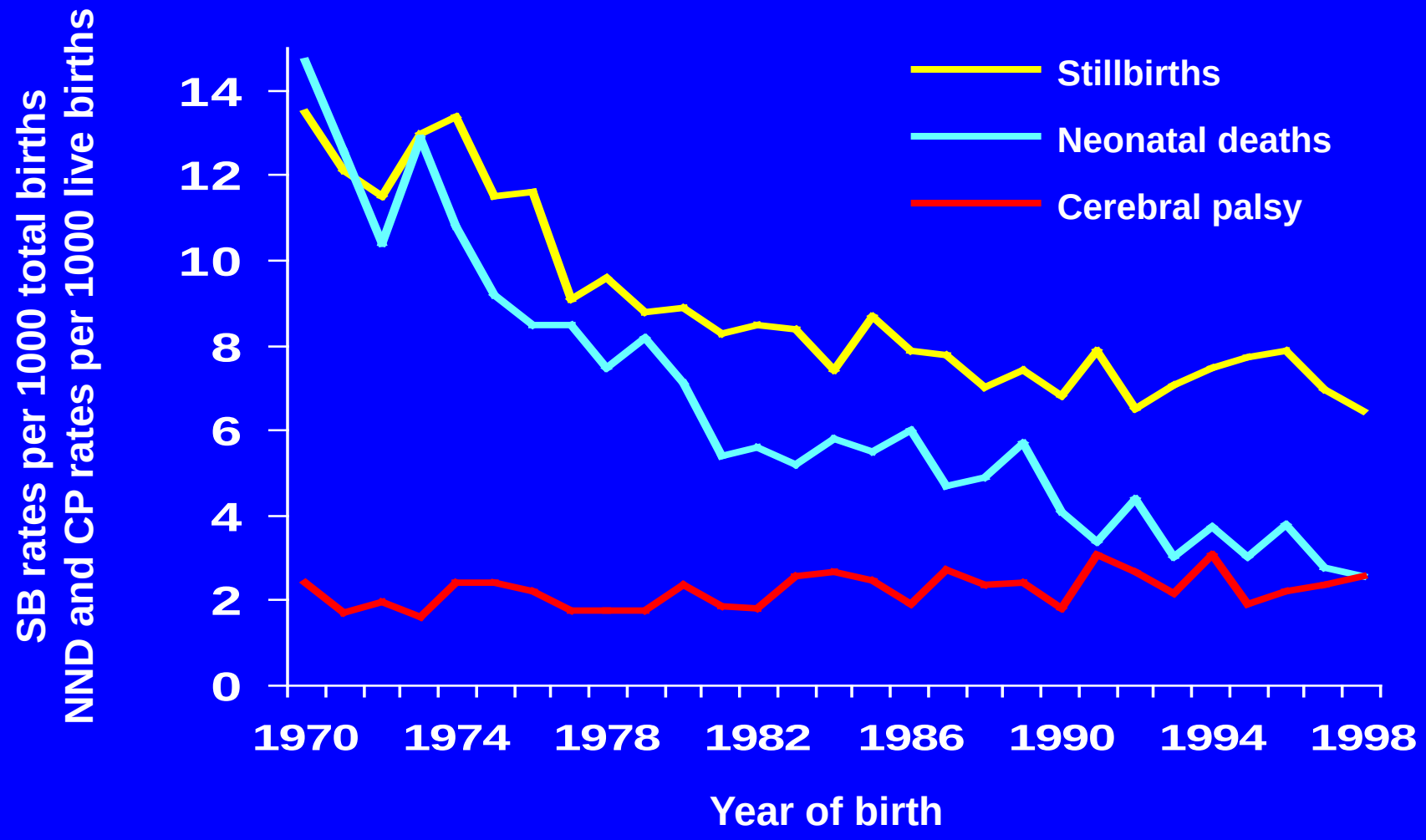
- Prevention of cot deaths
- Folate campaign for spina bifida
- Childhood vaccination coverage
- Anti-smoking programs
- Don’t Shake Your Baby
- STD, drug and alcohol programs

Trends in Overall CP Western Australia, 1956-1999

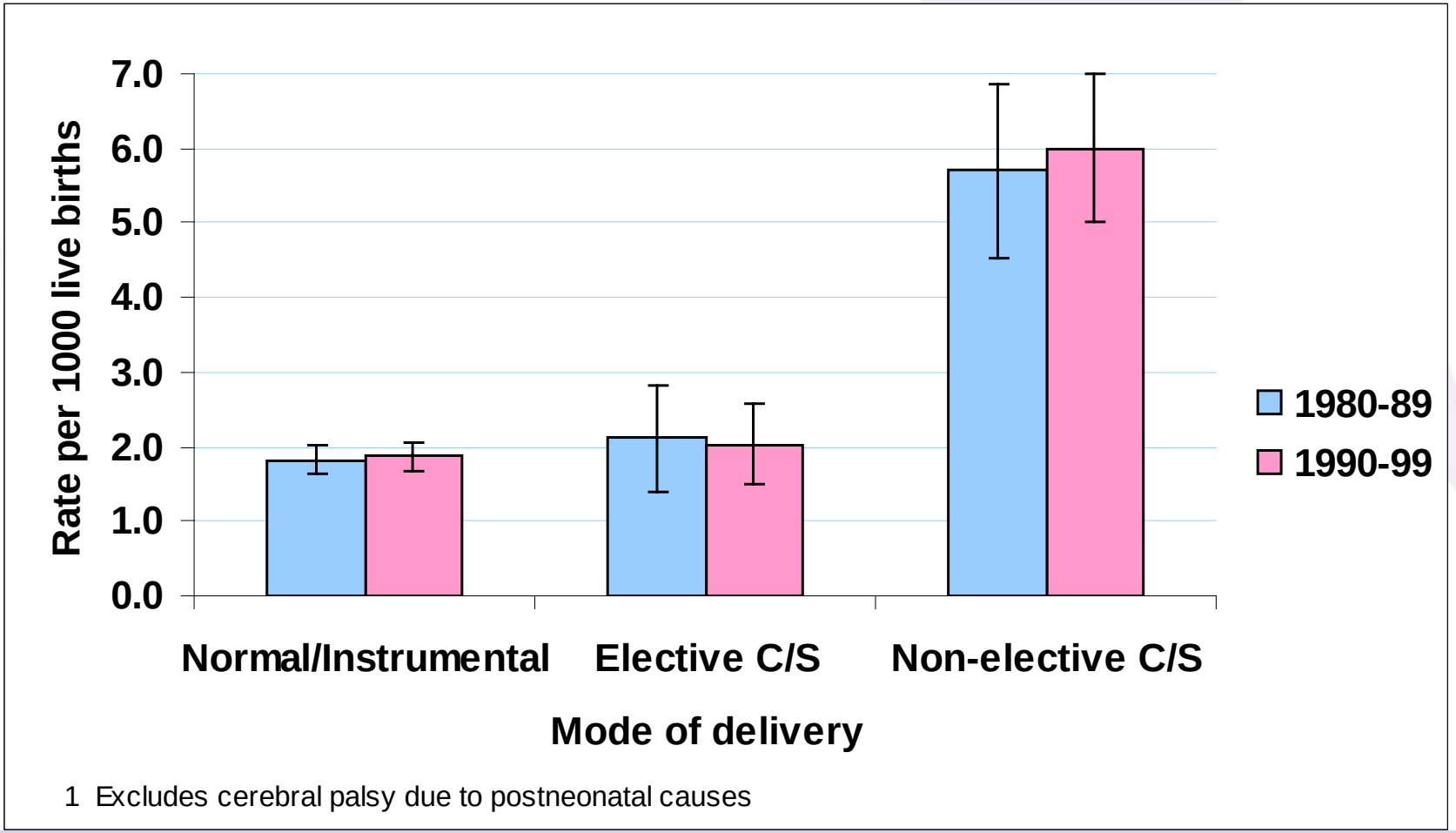


Source: Watson, Blair & Stanley: Report of WA CP Register to birth year 1999

Trends in cerebral palsy, stillbirths, and neonatal deaths, Western Australia, 1970-1998

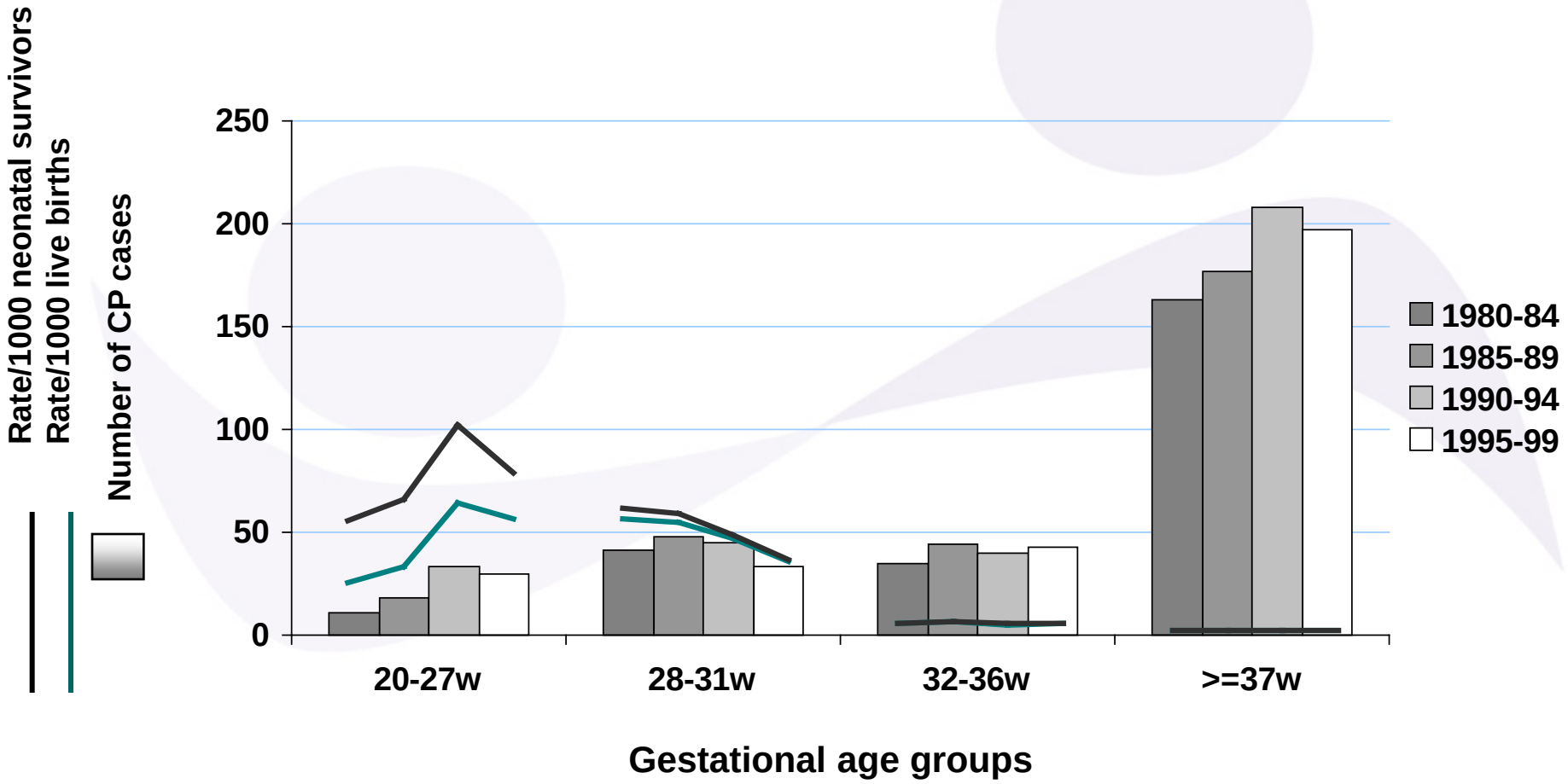


Total Cerebral Palsy[1] rates by Mode of Delivery, Western Australia, 1980-1999



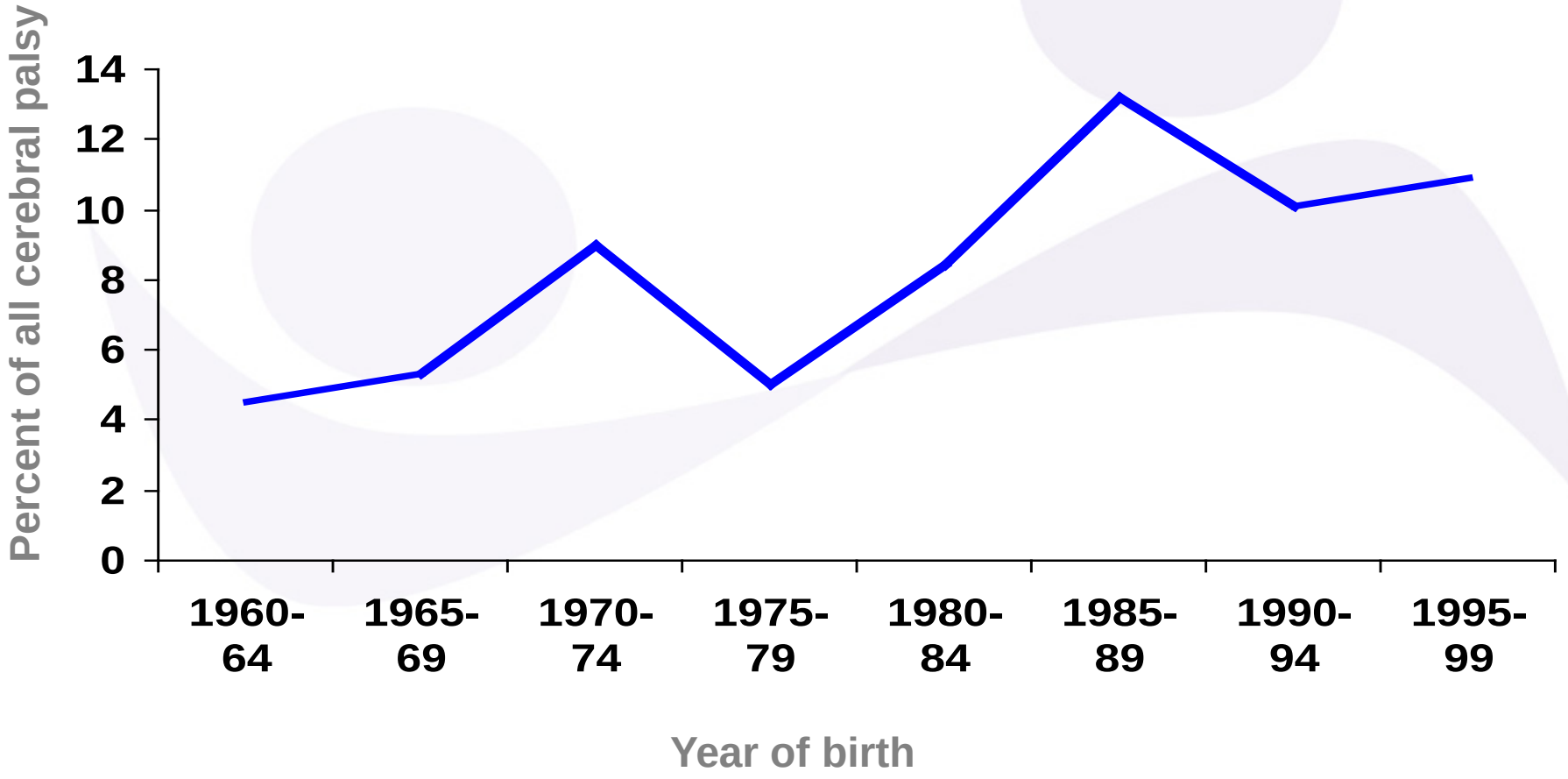
1 Excludes cerebral palsy due to postneonatal causes

Cerebral Palsy[1] Numbers and Rates by Gestational age in Western Australia, 1980-1999



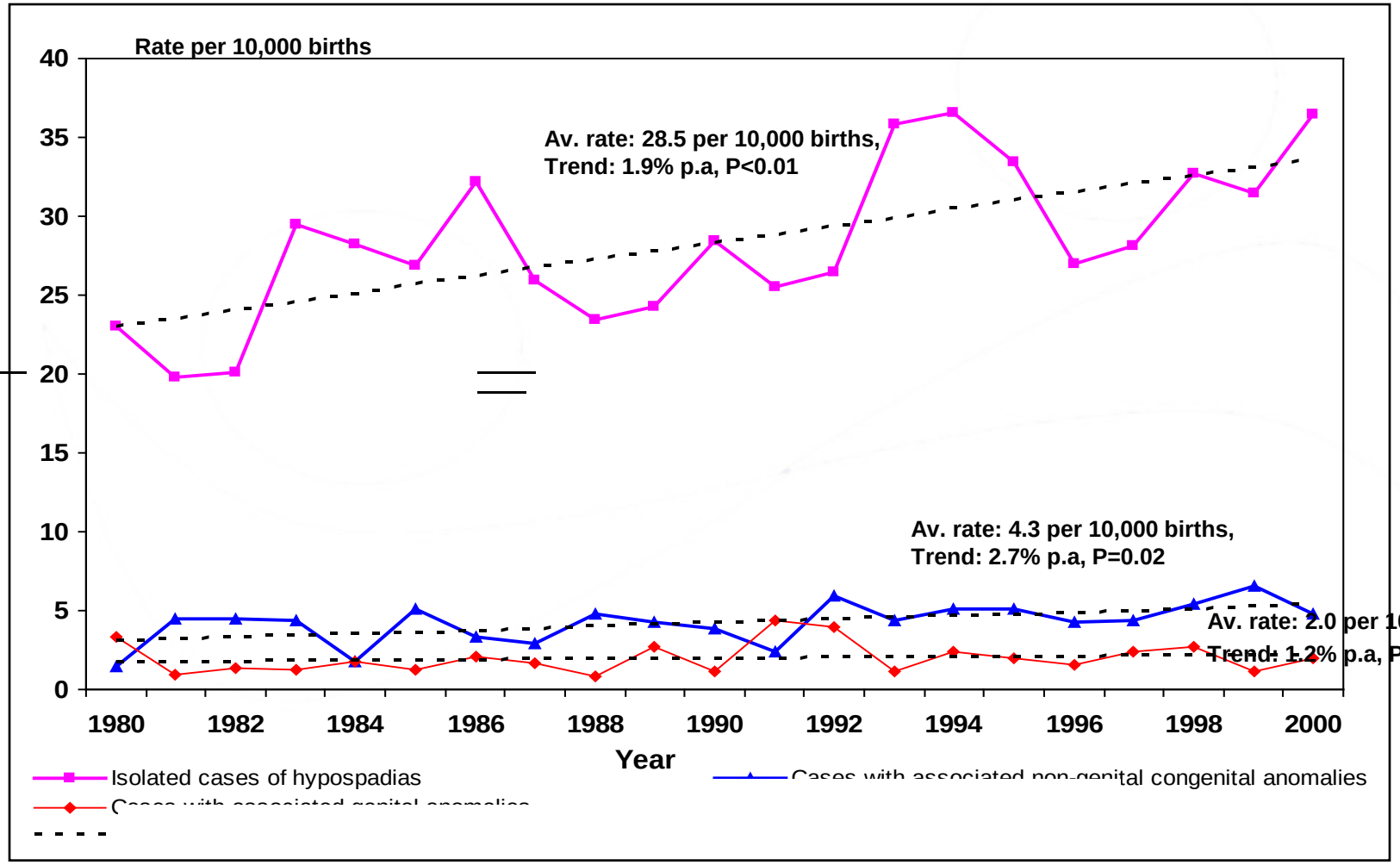
1 Excluding cerebral palsy due to postneonatal causes

Proportion of Cases of Cerebral Palsy* from Multiple Gestations, Western Australia, 1960-1999



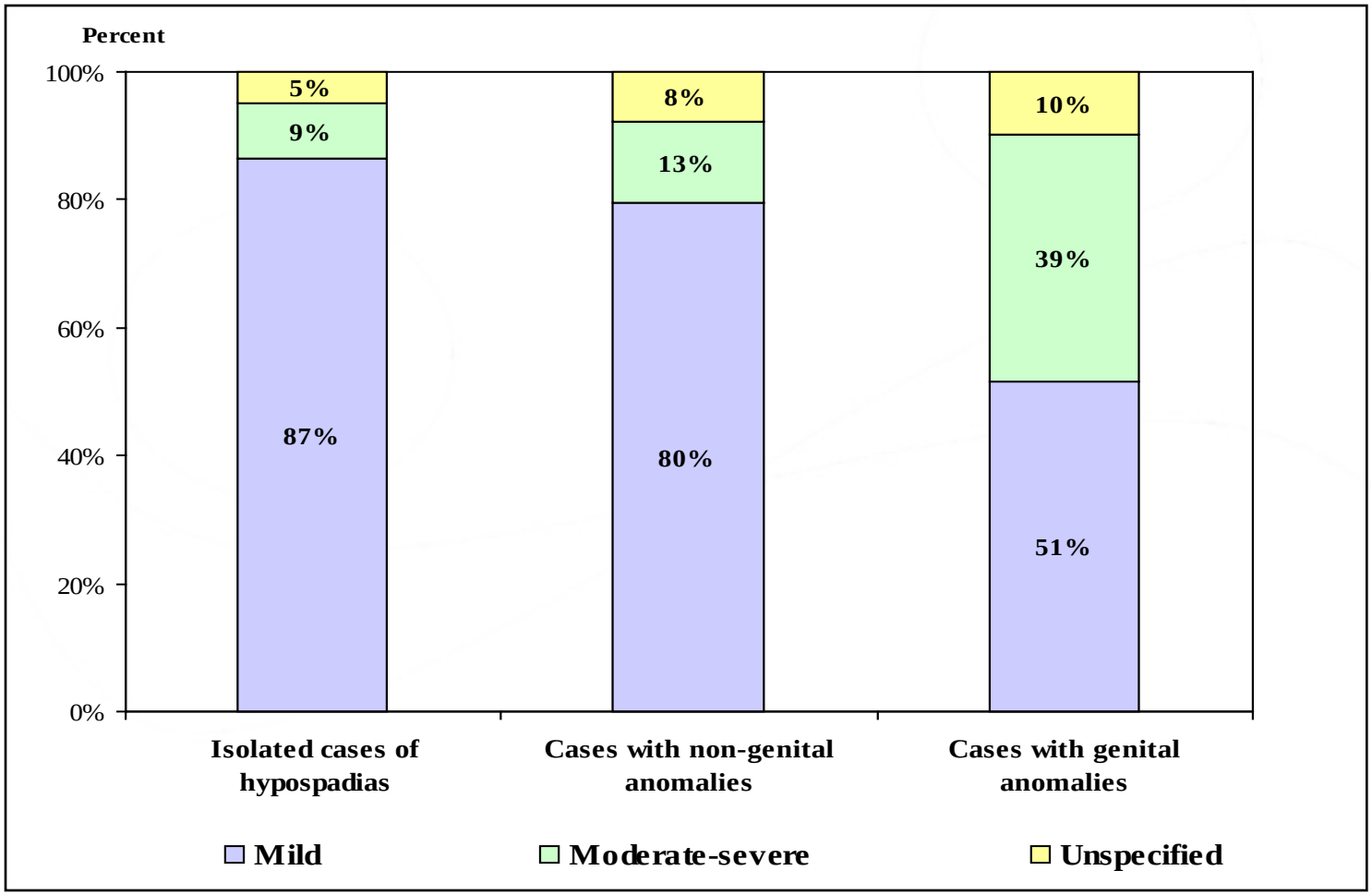
* Excludes cerebral palsy due to postneonatal causes

Trend in Prevalence of Hypospadias by Associated Congenital Anomalies



Source: Nassar, Bower & Barker. Accepted for pub. Am Journal Epi

Association of Hypospadias with other Congenital Anomalies and Degree-of-severity



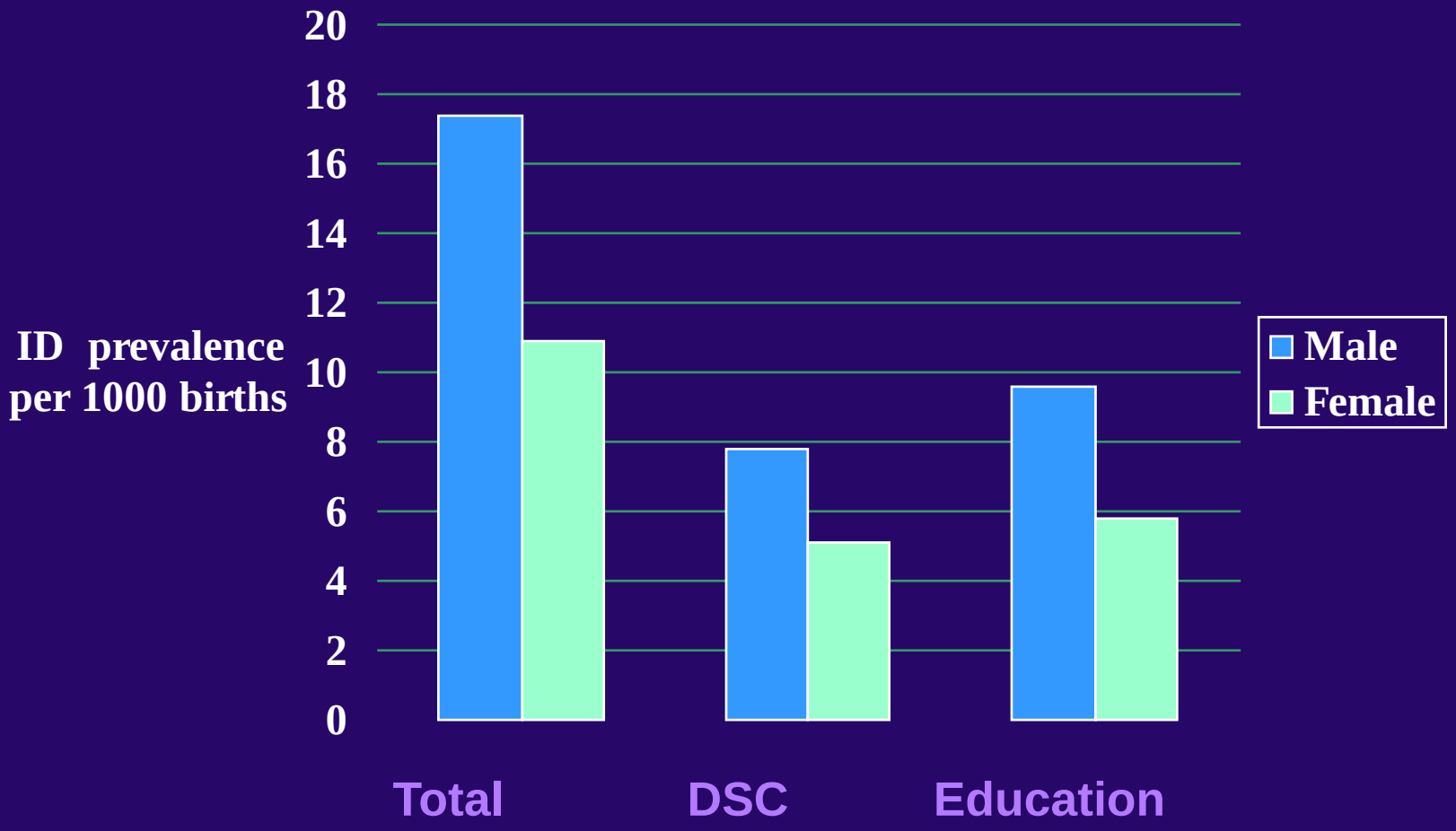
Source: Nassar, Bower & Barker. Accepted for pub. Am Journal Epi

Population Based Record Linkage Study
Juvenile Diabetes

- Increase in both Type 1 and Type 2
- Type 1: 11.3/100,000 1985 - 23.2/ in 2002
  All ages 0-14 years
- Type 2: 27% annual increase
- Risk factors
  - Increased maternal age
  - Birthweight (↑) / gestational age (↓)
  - Birth order (protective)
  - Urban > rural
  - Socioeconomic status (↑)

Source: Haynes et al 2004, 2006, 2007

Prevalence of intellectual disability by source of ascertainment and gender

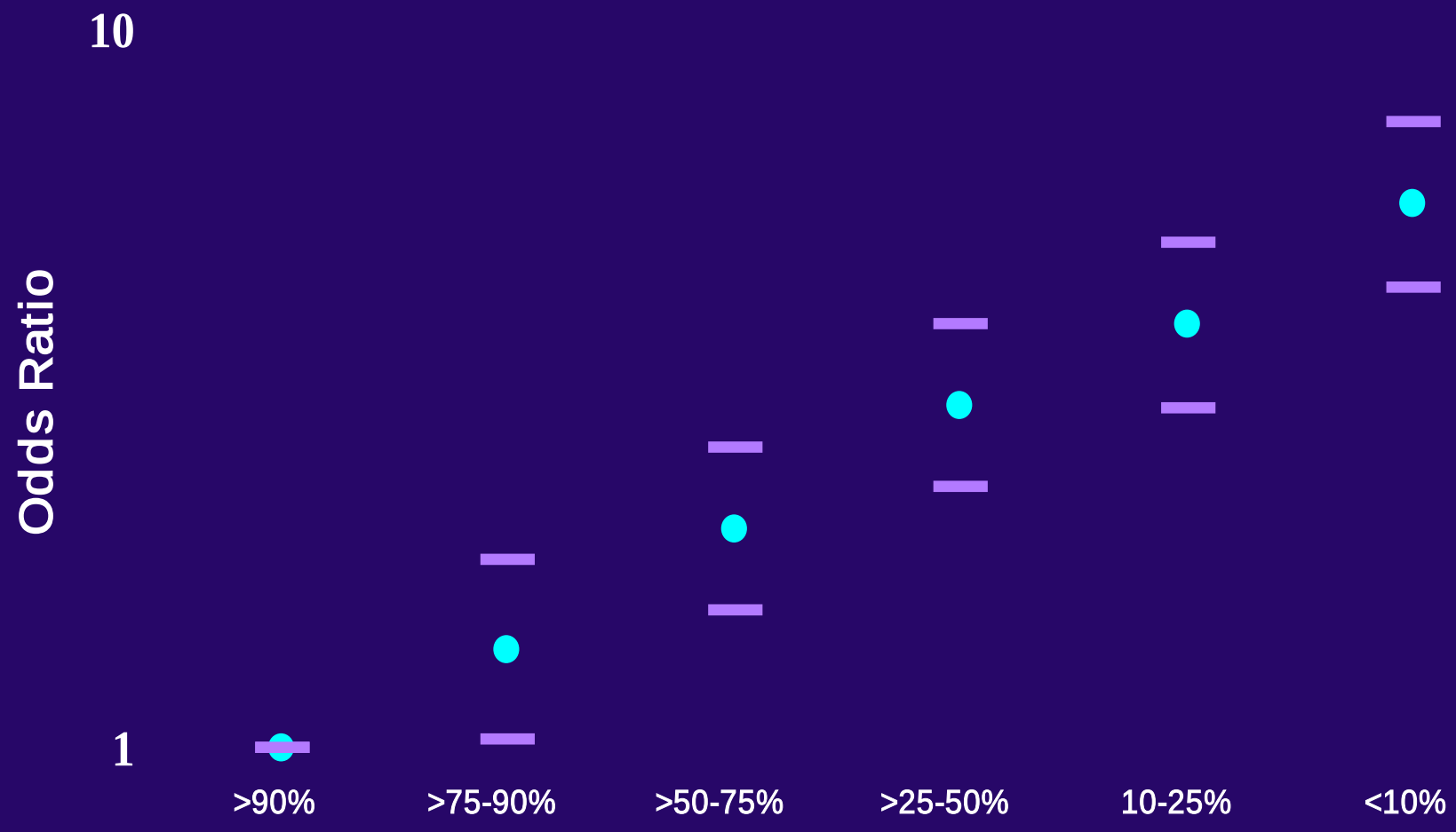


	Total	DSC	Education
Prevalence Ratio	1.6	1.5	1.7
95% CI	(1.5-1.7)	(1.4-1.7)	(1.5-1.8)

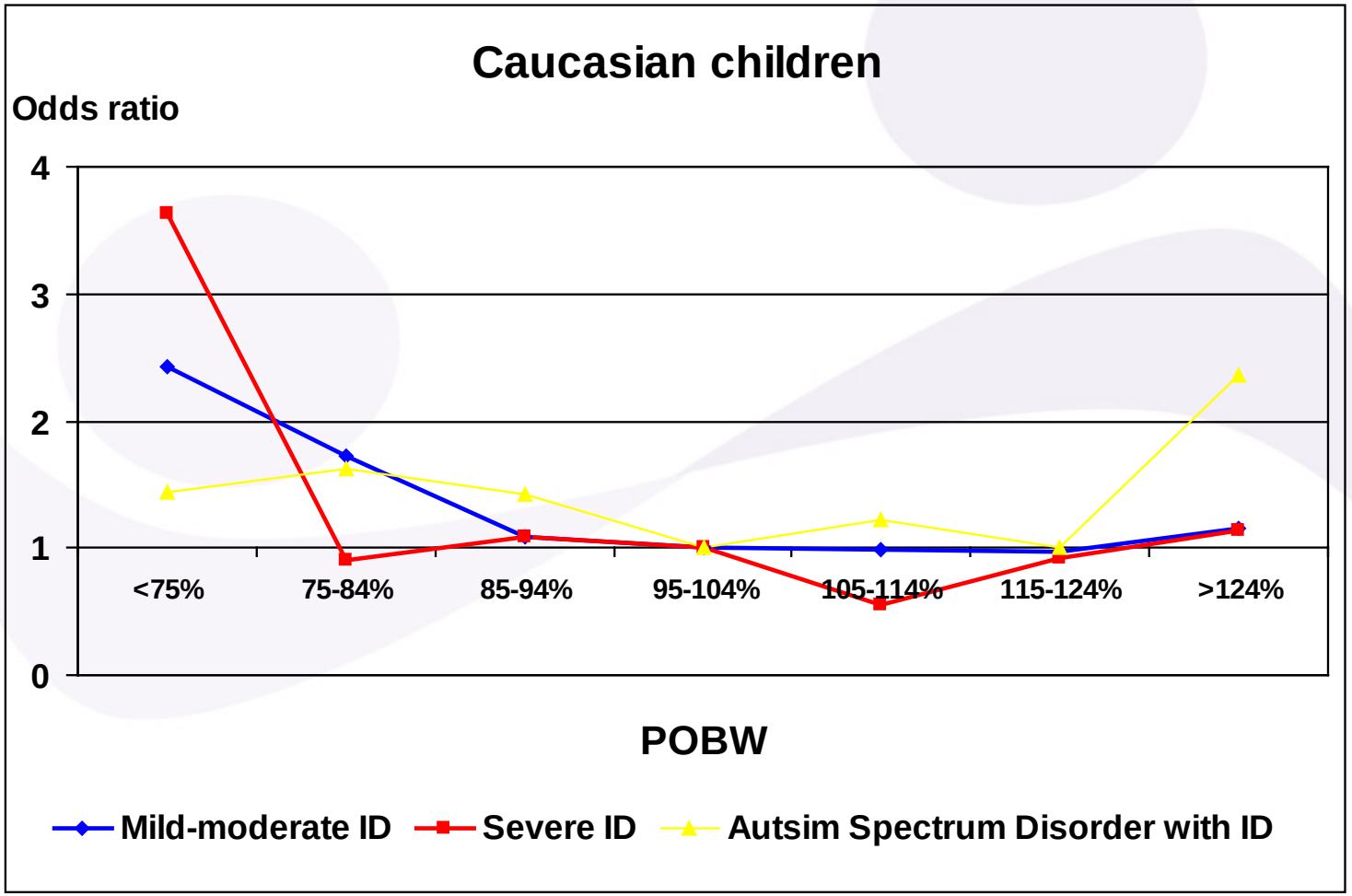
Mother <20 years compared with 25-29 years by ID category

Index of relative social disadvantage <10% compared with >90% by ID category

Mild-moderate ID
by index of education and occupation

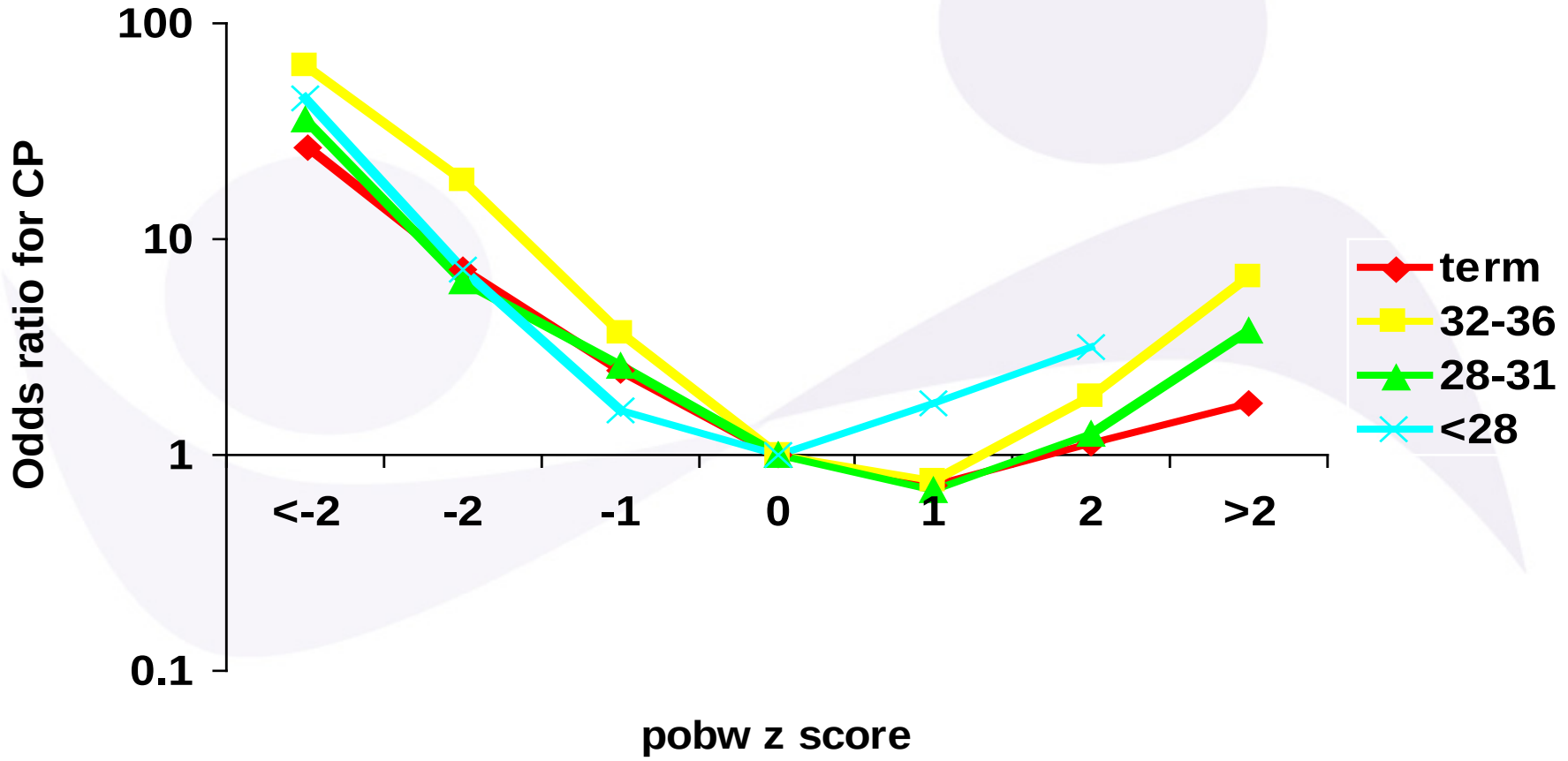


Odds ratio of fetal growth and intellectual disability in Caucasian children born in WA



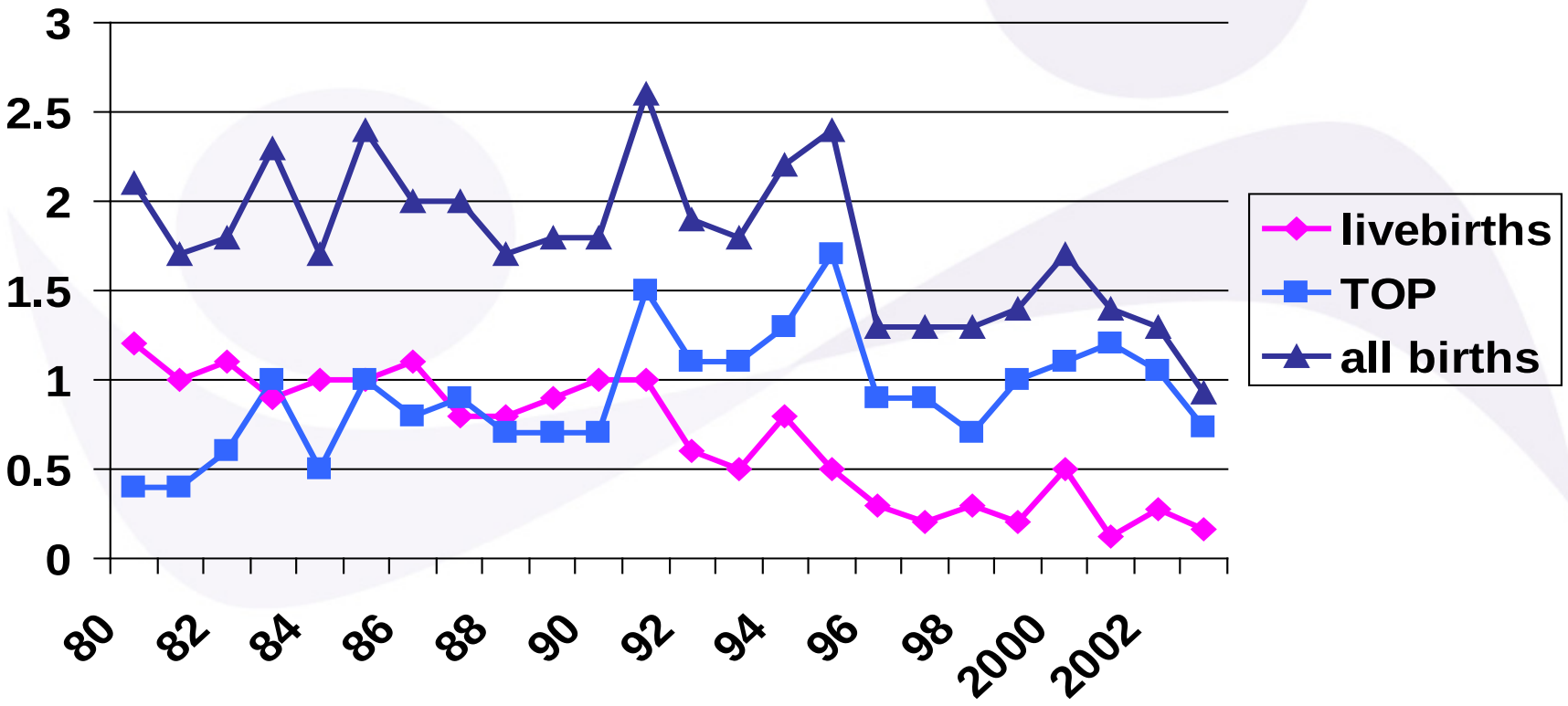
Source: Nassar et al unpublished data

OR* for CP in Singletons by Growth and Gestation of Delivery.



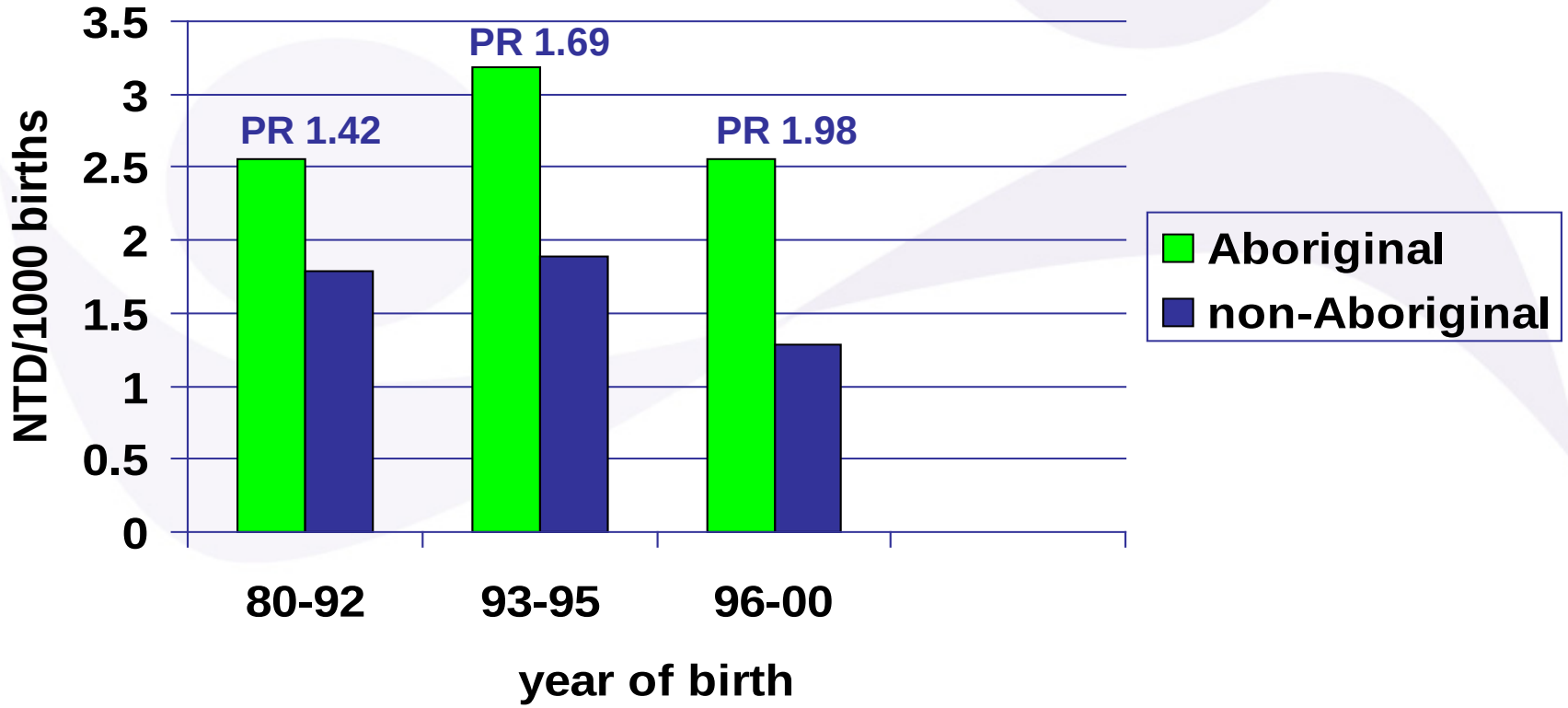
*relative pobw z score= 0 in gestational age stratum

Trends in NTD in WA



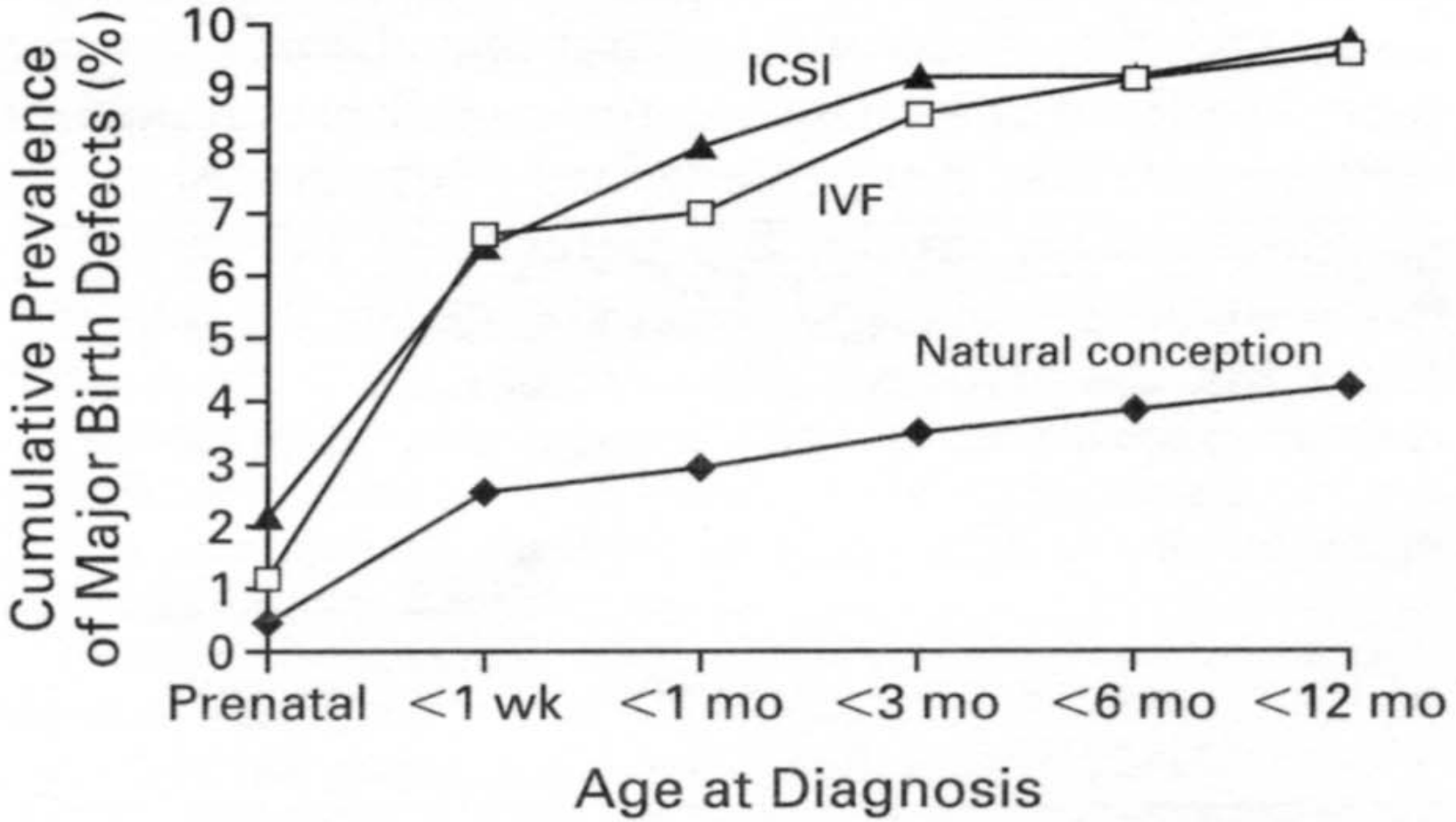
Source: Bower et al, Birth Defects Registry

NTD in Indigenous and Non-Indigenous infants by Grouped Years of Birth



Source: C Bower 2005

Cumulative Prevalence of Birth Defects after ICSI & IVF



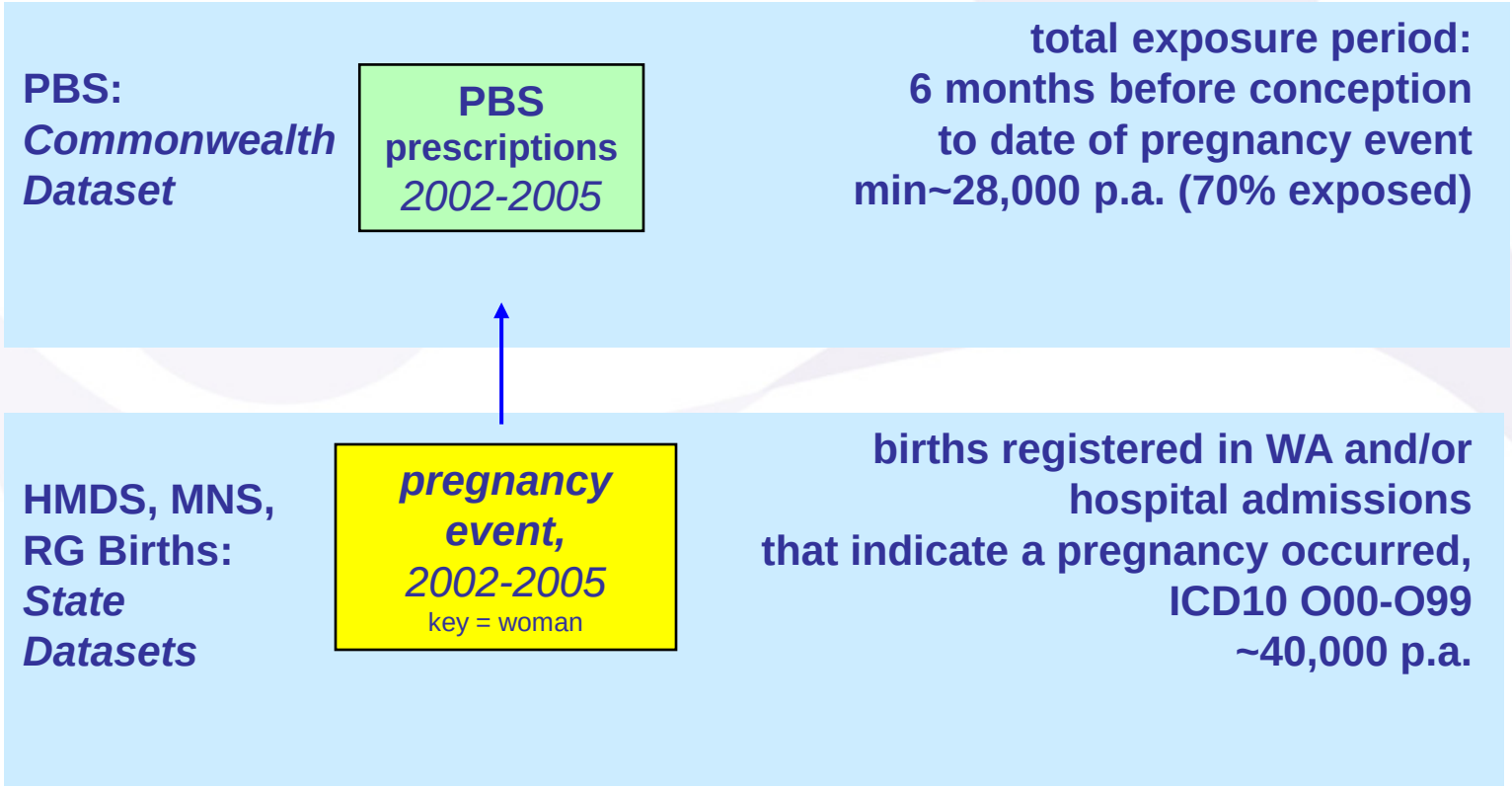
Source:Hansen, Kurinczuk, Bower & Webb 2002

2. The special case of pharmacovigilance

Urgency for Paediatric Pharmacovigilance

- Many drugs prescribed in pregnancy and childhood no RCT
- Many RCT too small or too short to evaluate harm
- Many RCT exclude co-morbidities, ages, others
- Some drugs (eg folate, antiepileptics, Vit A analogues) need post marketing surveillance

Data Linkage for Pharmacovigilance: Pregnancy



Source: Lyn Colvin TICHR Unpublished Data

Pharmacovigilance Initiative Possible Uses

- Product safety
- Therapeutic effect of drugs - how effective and if effective in all groups
- Drug interactions and their safety/adverse effects
- Therapeutic use of a drug - whether a drug is being prescribed properly and whether it is working
- Drug utilisation/ uptake - who is getting it and where
- New drugs replacing old ones - why, how, costs and consequences
- Trends and patterns in prescribing drugs

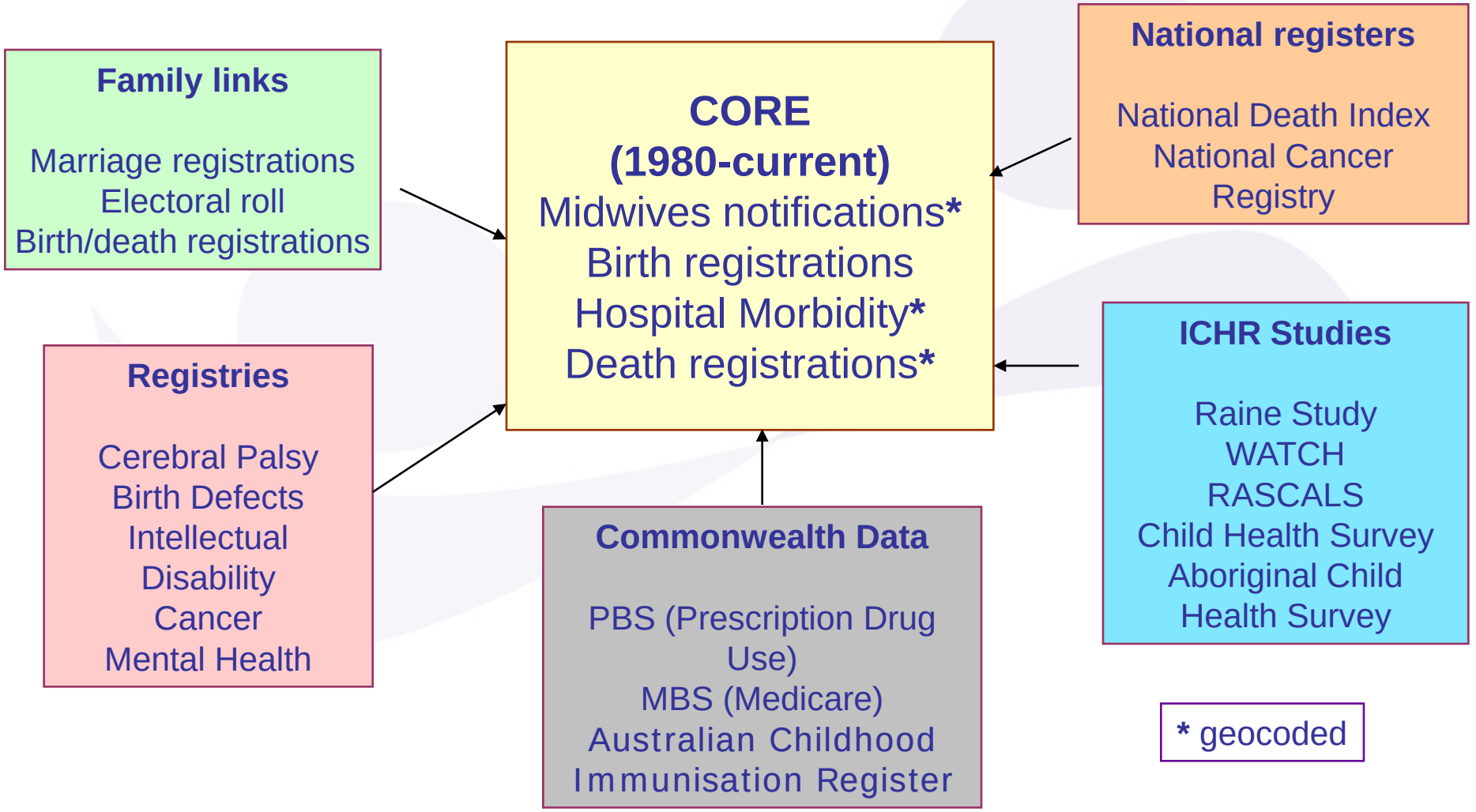
3. Ethical issues

Consent

- Consent is essential for all research involving participation of individuals
  - Questionnaires, interviews
  - Donate blood, tissues
  - Drug trials etc
- Not all research requires consent

WA Data Linkage Unit

MCHRDB 2004 Onwards



Bias

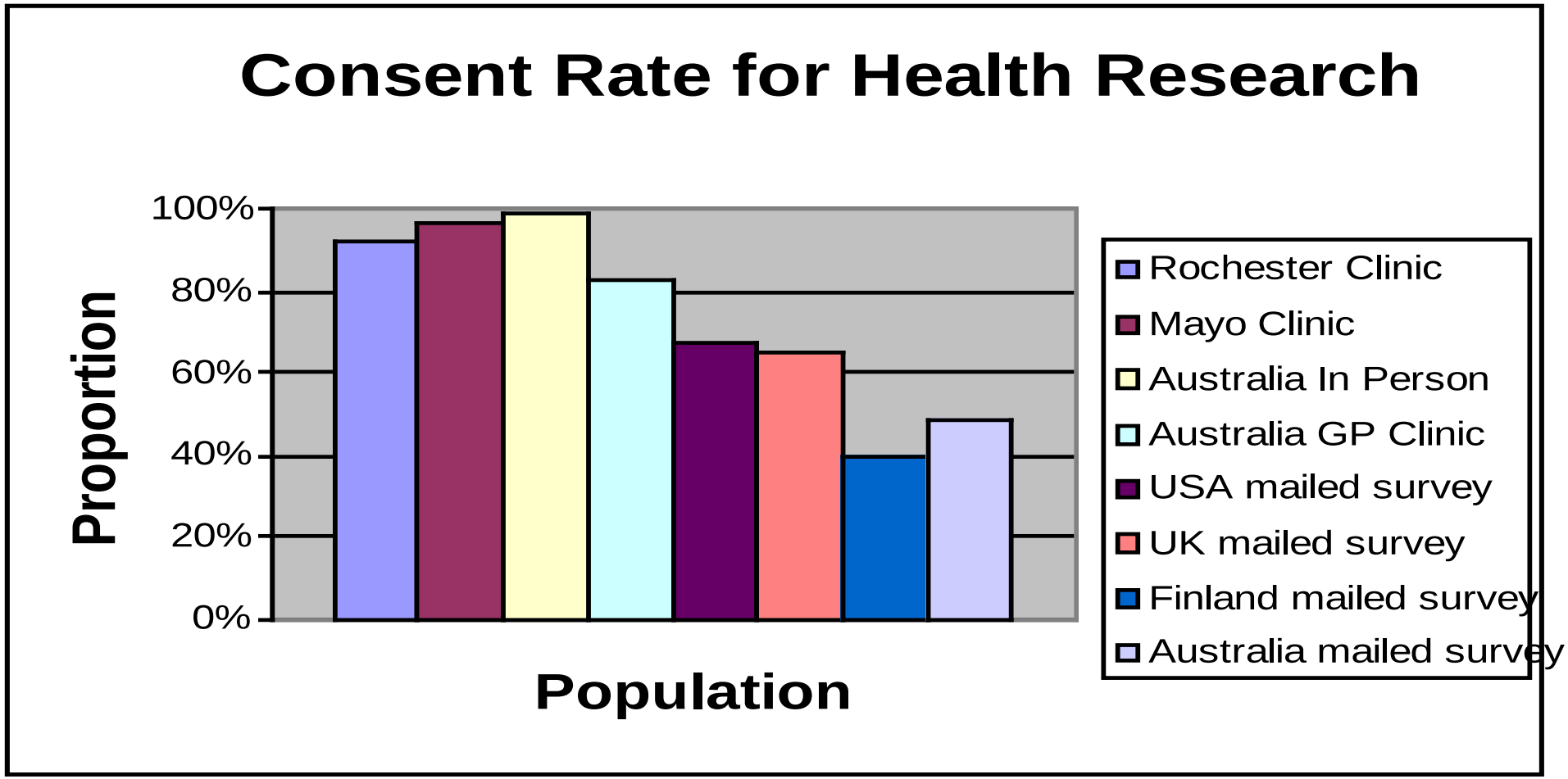
- Bias is the distortion of the true relationship between exposure and outcome due to flaws in either study design or analysis
- Can give wrong answers

Bias from Non-Participation

- Inability to trace/ contact (most common)
- Refusal (rare)

Both of these groups very different from participants

- Magnitude and direction not predictable
- Not quantifiable
- Explain differences in risks between studies
- Poor information for health services and epidemiological research


Consent Rate for Health Research
100%
80%
60%
40%
20%
0%
Proportion
Population
Rochester Clinic
Mayo Clinic
Australia In Person
Australia GP Clinic
USA mailed survey
UK mailed survey
Finland mailed survey
Australia mailed survey

New Yorker May 2003

Does TOP Increase the Risk of Later Breast Cancer?

- Recent meta analysis (53 studies)
- Retrospective studies with variable reporting & response rates RR=1.14(1.09-1.19)
- Record linking of abortion data to cancer register data RR=0.93(0.89-0.96)
- Comparisons of abortion registry & self report data
  - 24% women with breast cancer and
  - 27% women without breast cancer reported incorrectly that they had never had an induced abortion
  - 27% of women reporting a spontaneous abortion did not report it 20 years later

Source: Beral V et al. 2004

Impact of Informed Consent on Participation Bias

- Tu et al (2004) analysed the impact of informed consent on characteristics of participation in the Canadian Stroke Registry
- Overall participation rate of eligible patients was 39%
- Bias - lower in-hospital mortality rate among participants
- Expensive ($500,000 over 2 years for consent alone)
- Scientifically useless

Consent for Population Data & Record Linkage

Seeking consent is:

A) Not practical/feasible
   - Unable to contact 100% of the population (death, mobility)
   - Hugely expensive to contact and get consent

B) Poor science
   - Variable participation - significant bias
   - Poor data on exposures - e.g. recall bias

USA - HIPAA

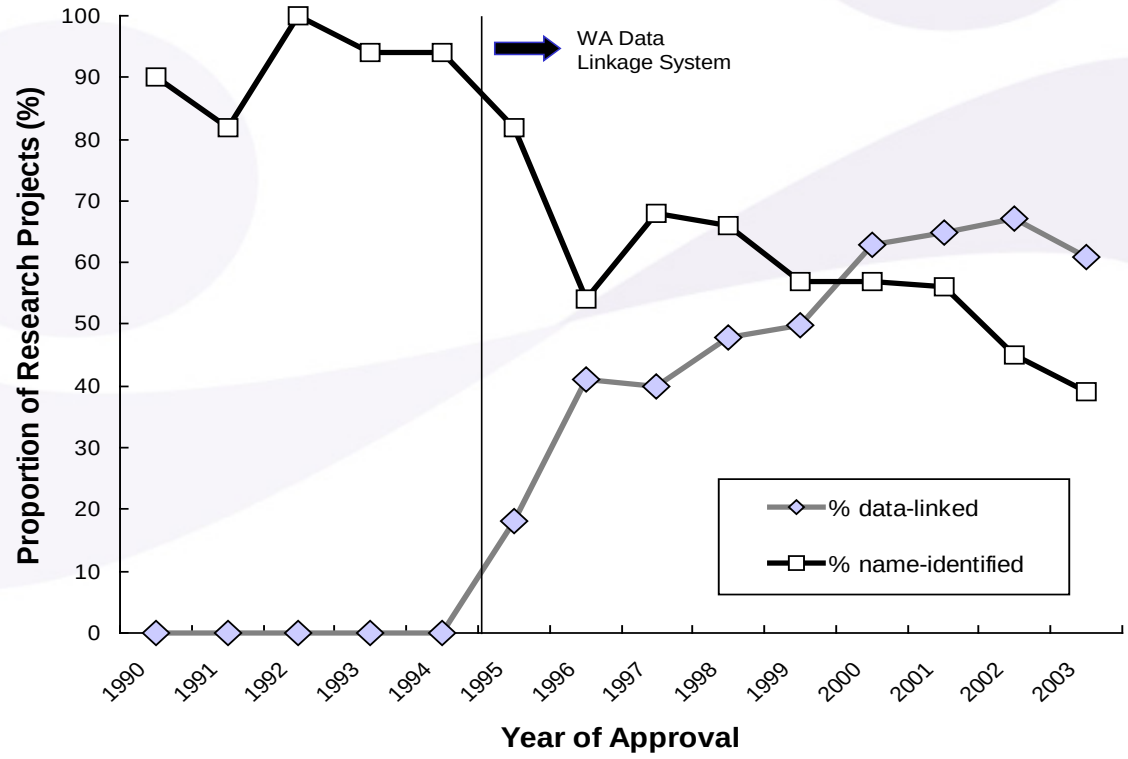
"As in Europe, any potential social benefits of epidemiological research were discounted in favor of privacy. This judgment seemed to be founded on the premise that no one ordinarily needs to see a medical record except the patient's personal physician. This, of course, is neither true nor desirable if we are to deliver effective and efficient integrated medical care."

L. Joseph Melton MD
Mayo Clinic

Source: NEJM Vol 337 1997

Proportion of Ethics Approved Research Projects using Name Identified & Data Linked Administrative Health Information WA 1990-2003

Figure Proportions of ethics-approved research projects (N=408) using name-identified and data-linked administrative health information in Western Australia 1990-2003



Source: Trutwein, Holman & Rosman (2006)

Our Health System Needs Effective Evaluation

- Spiraling costs of care
- Increase complex diseases
- New technologies, drugs - harmful side effects
- Patient expectations
- Concerns over safety
- Poor data for service planning

4. Modernity’s paradox and the imperative for good data

Modernity's Paradox

- Increasing prosperity
- Increasing problems for children and youth
- Increasing inequalities in outcomes and opportunities

Source: Keating & Hertzman 1999

Indicators of Poor Developmental Health which are Increasing in Australian Children and Youth

Health Outcomes

- Low birth weight
- Complex diseases (asthma, diabetes, obesity)
- Mental Health problems, suicide

Lifestyle risk factors

- Child abuse/neglect/domestic violence
- Behavioural problems, substance abuse

Others

- Juvenile crime
- Learning disorders
- Disabilities (intellectual, physical)

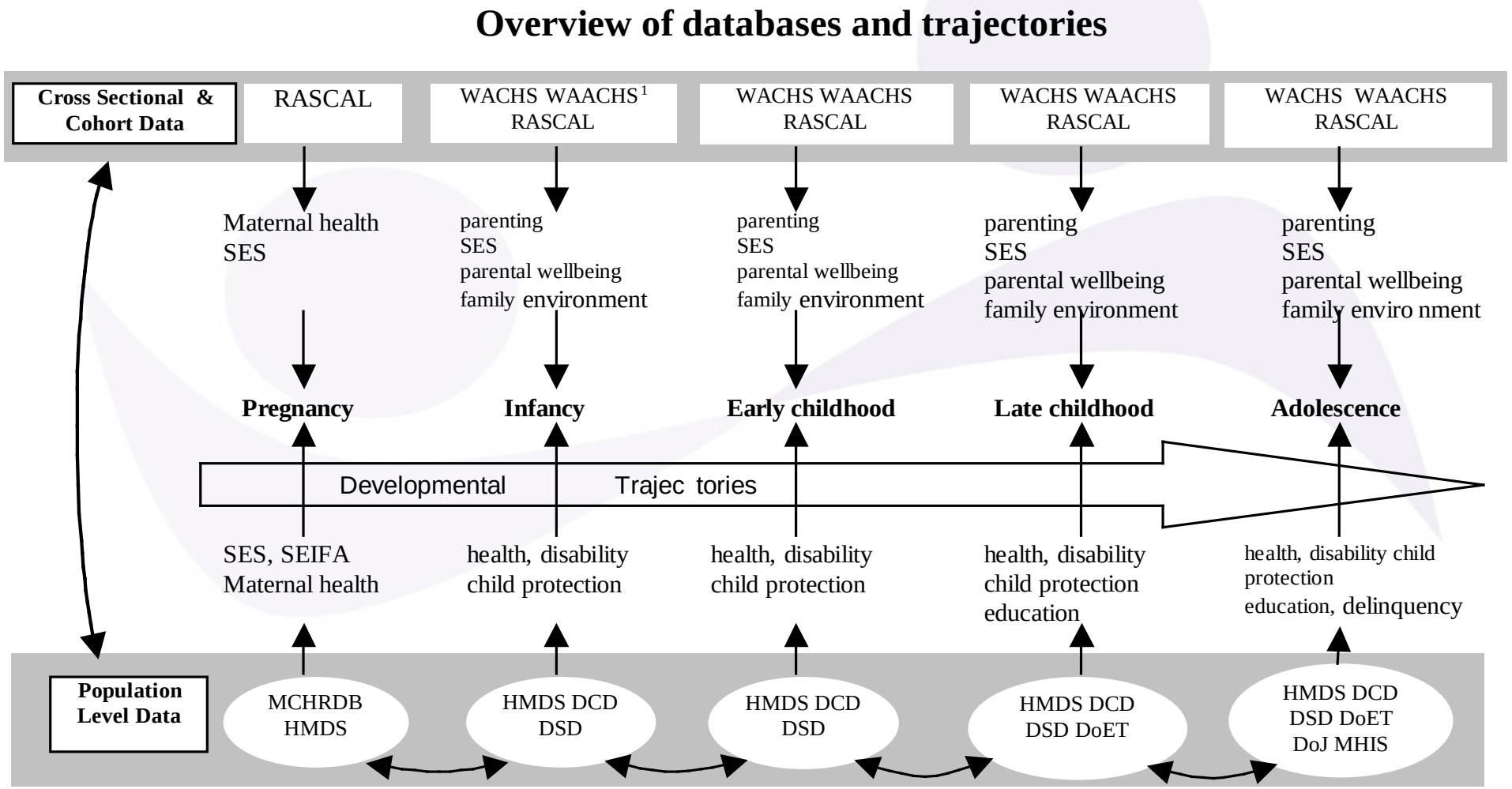
Source: Stanley, 2000 Millennium Year Book

Trends in Problems Affecting Children & Youth in Today's World

- Many are increasing in incidence
- Complex problems (eg mental health, obesity)
- Demand complex information to monitor, study & prevent them
- Costly to treat & manage
- Crisis in child & youth services (health, mental health, education & crime)
- Research in silos
- Services in silos

Bad Parenting….

MCHRDB & ARC Linkage Grant



“ In the late 20th century, scholars and politicians posed a key question ‘What desires and needs do you have as an autonomous rights bearing person to privacy, liberty and free enterprise?’ Now it is important to ask another kind of question ‘What kind of community do you want and deserve to live in, and what personal interests are you willing to forgo to achieve a good and healthy society?’ “

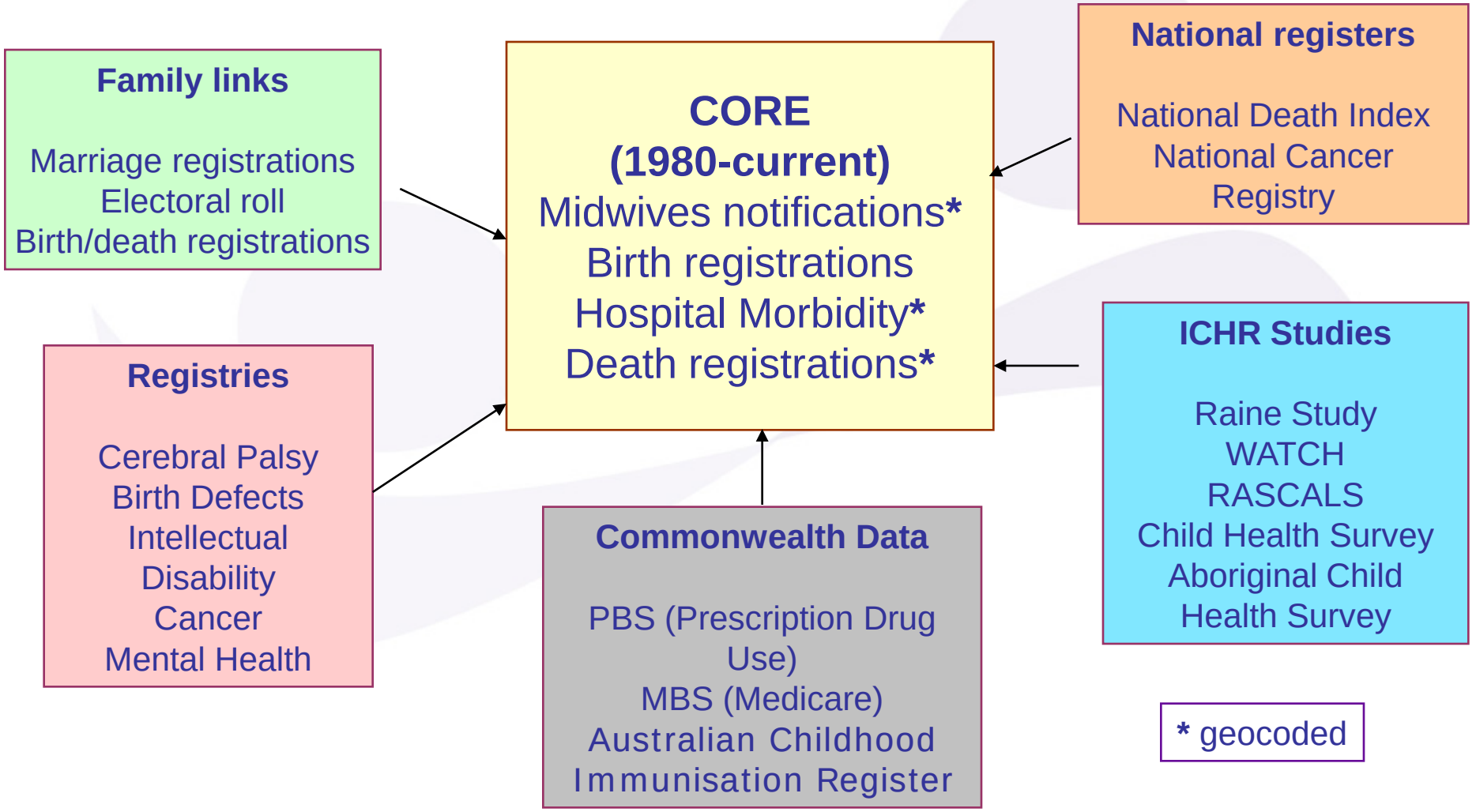
Prof Lawrence O Gostin 2004
University of Georgetown

Rationale for ARACY

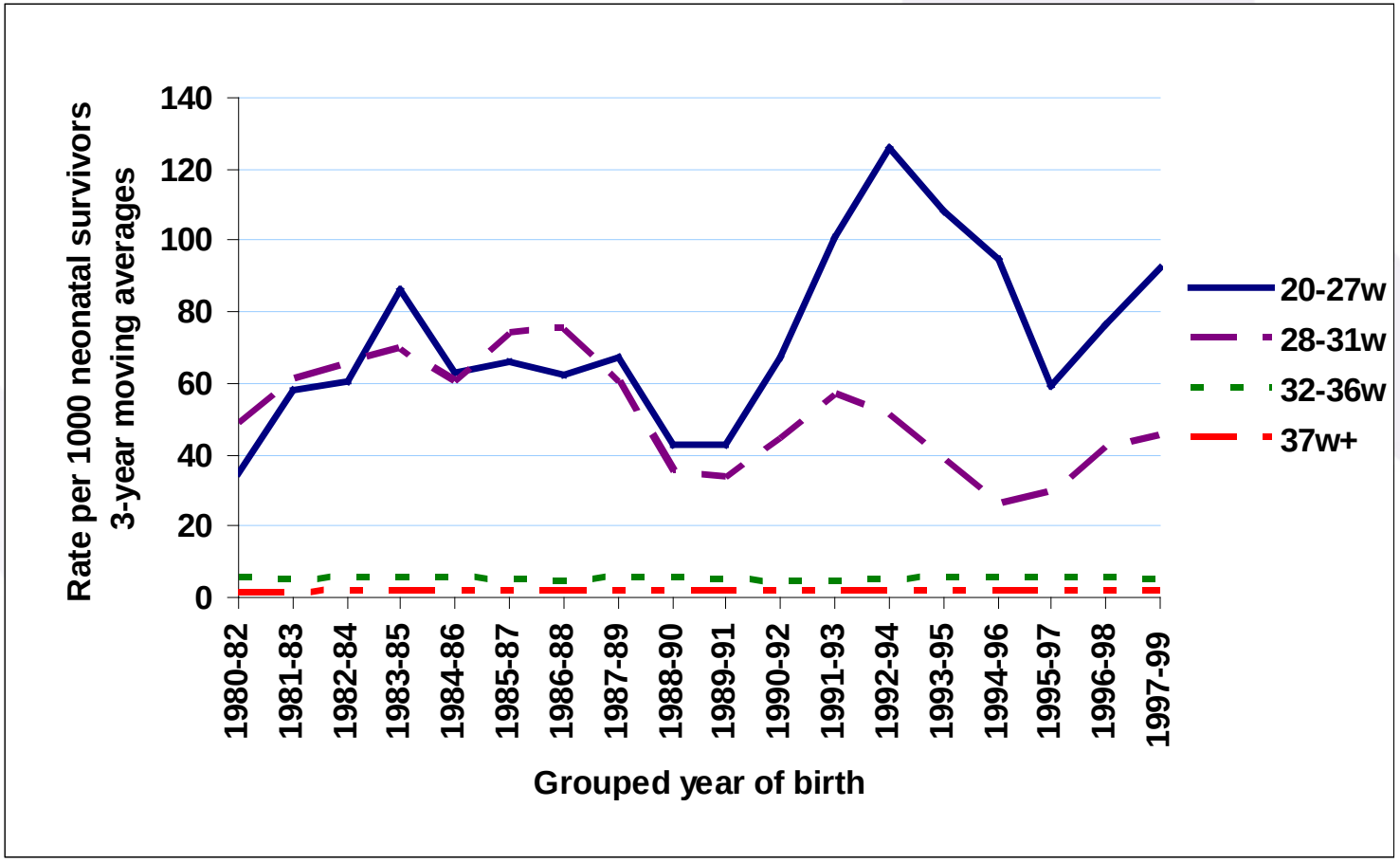
- Rise in complex problems (eg mental health, obesity)
- Demand complex information to monitor, study & prevent them
- Research is fragmented, done in separate silos and does not inform solutions
- Policy in silos, not using research
- Most research and policy ignore major socioeconomic drivers of poor outcomes

WA Data Linkage Unit

MCHRDB 2004 Onwards

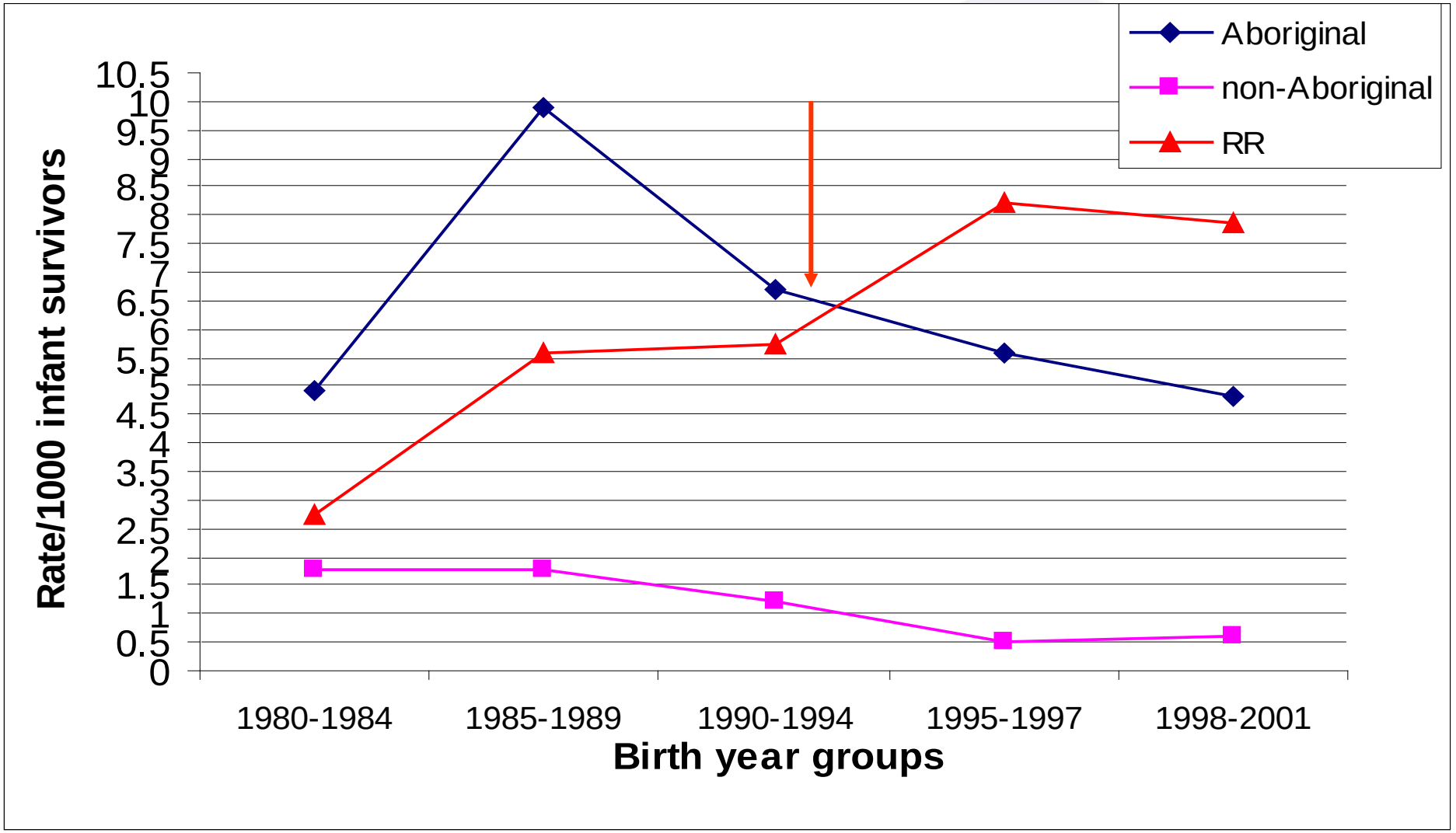


Cerebral Palsy by Gestational age in Western Australia, 1980-1999



Source: Watson, Blair & Stanley: Report of WA CP Register to birth year 1999

SIDS by Aboriginal status and Birth Year Groups, WA births 1980-2001



Source: J Freemantle 2004

Privacy Concerns

- Abuse, particularly genetic risk data, by insurers or employers
- Sensitive information on individuals given out without their knowledge
- Government control of personal data
- Prefer consent for record linkage
- However, in focus groups:(McCallum et al 1993, Kelman 2005)
  - Strong support for public good research
  - Trusted research in universities
  - Acknowledged low risk

UK Privacy & Medical Research

Personal data for public good: using health information in medical research

- Increased complex laws/regulations
- Variable interpretation
- Many projects blocked/delayed
- Increase in costs
- Poor public awareness of value and methods of research

Commentary Lancet, 2006

Source: Academy of Medical Sciences, 2006